**PCT** WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61N 1/40, A61H 7/00 — A1

(11) International Publication Number: WO 98/05380

(43) International Publication Date: 12 February 1998 (12.02.98)

(21) International Application Number: PCT/US97/13608

(22) International Filing Date: 4 August 1997 (04.08.97)

(30) Priority Data:
60/023,377 6 August 1996 (06.08.96) US

(60) Parent Application or Grant
(63) Related by Continuation
US 60/023,377 (CIP)
Filed on 6 August 1996 (06.08.96)

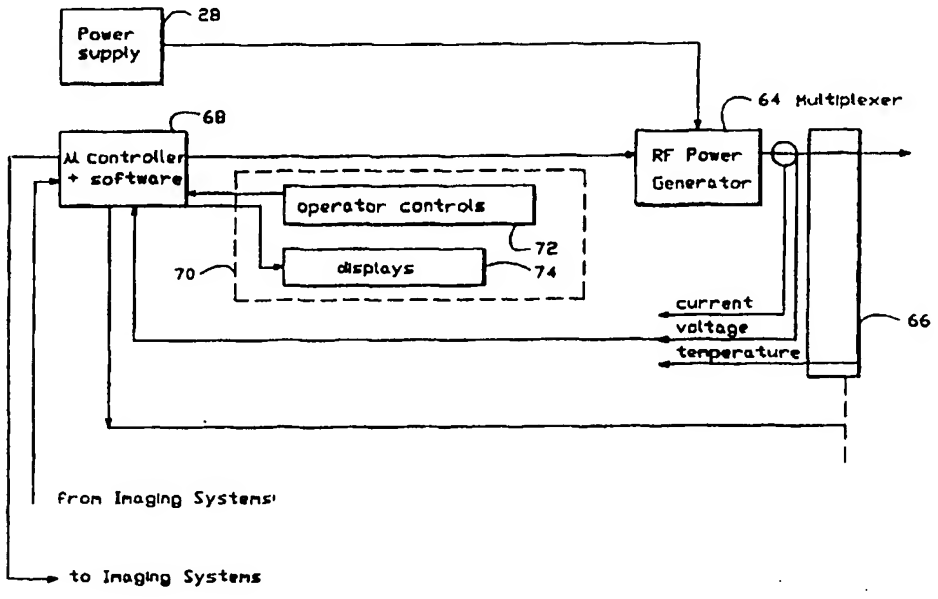
(71)(72) Applicant and Inventor: KNOWLTON, Edward, W. [US/US]; 5478 Blackhawk Drive, Danville, CA 94506 (US).

(74) Agent: DAVIS, Paul; Wilson, Sonsini, Goodrich & Rosati, 650 Page Mill Road, Palo Alto, CA 94304-1050 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
*With international search report.*

(54) Title: METHOD FOR TIGHTENING SKIN




(57) Abstract

A method for tightening skin provides for a modification of tissue impedance. An electromagnetic energy delivery device, with an energy delivery surface, is positioned with at least a portion of the energy delivery surface on a skin surface. Electromagnetic energy is delivered from the energy delivery surface through the skin surface, through the skin and to an underlying collagen containing tissue. An impedance of at least a portion of the skin or the underlying collagen containing tissue is modified. At least a portion of the collagen containing tissue is contracted and the surface of the skin is tightened.

cited in the European Search Report of EP 04 76 9467.9
Your Ref.: M&E 110.021S0301

*FOR THE PURPOSES OF INFORMATION ONLY*

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| AL | Albania | ES | Spain | LS | Lesotho | SI | Slovenia |
| AM | Armenia | FI | Finland | LT | Lithuania | SK | Slovakia |
| AT | Austria | FR | France | LU | Luxembourg | SN | Senegal |
| AU | Australia | GA | Gabon | LV | Latvia | SZ | Swaziland |
| AZ | Azerbaijan | GB | United Kingdom | MC | Monaco | TD | Chad |
| BA | Bosnia and Herzegovina | GE | Georgia | MD | Republic of Moldova | TG | Togo |
| BB | Barbados | GH | Ghana | MG | Madagascar | TJ | Tajikistan |
| BE | Belgium | GN | Guinea | MK | The former Yugoslav Republic of Macedonia | TM | Turkmenistan |
| BF | Burkina Faso | GR | Greece | | | TR | Turkey |
| BG | Bulgaria | HU | Hungary | ML | Mali | TT | Trinidad and Tobago |
| BJ | Benin | IE | Ireland | MN | Mongolia | UA | Ukraine |
| BR | Brazil | IL | Israel | MR | Mauritania | UG | Uganda |
| BY | Belarus | IS | Iceland | MW | Malawi | US | United States of America |
| CA | Canada | IT | Italy | MX | Mexico | UZ | Uzbekistan |
| CF | Central African Republic | JP | Japan | NE | Niger | VN | Viet Nam |
| CG | Congo | KE | Kenya | NL | Netherlands | YU | Yugoslavia |
| CH | Switzerland | KG | Kyrgyzstan | NO | Norway | ZW | Zimbabwe |
| CI | Côte d'Ivoire | KP | Democratic People's Republic of Korea | NZ | New Zealand | | |
| CM | Cameroon | | | PL | Poland | | |
| CN | China | KR | Republic of Korea | PT | Portugal | | |
| CU | Cuba | KZ | Kazakstan | RO | Romania | | |
| CZ | Czech Republic | LC | Saint Lucia | RU | Russian Federation | | |
| DE | Germany | LI | Liechtenstein | SD | Sudan | | |
| DK | Denmark | LK | Sri Lanka | SE | Sweden | | |
| EE | Estonia | LR | Liberia | SG | Singapore | | |

SDOCID: <WO_____9805380A1_I_>

# METHOD FOR TIGHTENING SKIN

## BACKGROUND OF THE INVENTION

### Field of the Invention

This invention relates generally to a method for contracting collagen containing tissue and tightening skin, and more particularly, to a method for tightening skin by modifying the impedance and/or the thermal conductivity of tissues.

### Description of Related Art

The human skin is composed of two elements: the epidermis and the underlying dermis. The epidermis serves as a biological barrier to the environment. In the basilar layer of the epidermis, pigment-forming cells called melanocytes are present. They are the main determinants of skin color.

The underlying dermis provides the main structural support of the skin. It is composed mainly of an extracellular protein called collagen. Collagen is produced by fibroblasts and exists as a triple helix with three polypeptide chains that are connected with heat labile and heat stable chemical bonds. When collagen is heated, alterations in the physical

properties of this protein occur at a characteristic temperature. This structural transition occurs in a manner analogous to the melting of a crystal. However, just as there is a "melting" temperature, there is a "shrinkage" temperature. The shrinkage of collagen is the basis for the technology and applications discussed in this presentation.

Soft tissue contraction is a biophysical phenomenon that occurs at cellular and molecular levels. Molecular contraction or denaturization of collagen involves the application of an energy source which results in the breaking of the heat labile bonds of the triple helix. As a result the longitudinal axis of the molecule contracts. This is essentially an immediate extracellular process, whereas cellular contraction requires a lag period for the migration and multiplication of fibroblasts into the wound as provided by the wound healing sequence. These cells differentiate into contractile myofibroblasts and are the source of cellular soft tissue contraction. Following cellular contraction, collagen is laid down as a static supporting matrix in the tightened soft tissue structure. Subsequent contraction can then be achieved by the molecular denaturization of collagen.

For example, tissue shrinkage with the denaturization of collagen occurs in second degree burns and is typically applied as a standard thermal gradient that is hotter on the surface and cooler in the underlying dermis. In these burn patients, cellular contraction and partial denaturization of dermal collagen results in a tightening effect on the skin. In contrast to the standard thermal gradient of a burn, the present invention provides a means to apply a reverse thermal gradient in which the skin's underlying collagen-containing layers are heated instead of the epidermis. Contraction of the skin and underlying soft tissue is possible without ablation or a second degree burn with its inherent blistering and





ISDOCID: <WO_____9805380A1_I_>

pigmentary irregularities. In a broader context, a reverse thermal gradient can also be described as a reverse gradient of collagen contraction in which collagen is preferentially contracted within a target tissue regardless of its relationship to a surface structure. Unwanted thermal effects and collagen contraction on adjacent soft tissue structures are avoided. Because collagen is found in tendon, bone, cartilage and all other connective tissue throughout the body, reverse thermal gradient contraction of collagen tissue can have many applications.

The selective induction of the basic wound healing process serves as the basis for the second major application of the present invention. In higher developed animal species, the wound healing response to injury involves an initial inflammatory process that subsequently leads to the deposition of scar tissue. The initial inflammatory response consists of the infiltration by white blood cells or leukocytes that dispose of cellular debris. Seventy-two hours later, proliferation of fibroblasts at the injured site occurs. These cells then produce scar collagen that functions as the main structural support of a healed wound. The deposition and subsequent remodeling of this nascent scar matrix provides the means to alter the consistency and geometry of soft tissue for both aesthetic and reconstructive purposes.

There exists an aesthetic need to contract skin without the scars, surgical risks or pigmentary side effects of commonly employed techniques. These techniques include surgical resection of skin and the use of lasers and chemical peels to burn the skin and achieve a tighter, more youthful appearance. Understandably, many patients are hesitant to subject themselves to these procedures, even though an overall aesthetic improvement is likely.





BNSDOCID: <WO_____9805380A1_I_>

heat. Heat generated in the tissue around the electrode is influenced by several factors: distance from the electrode, RF current intensity and frequency, tissue impedance, shrinkage temperature (Ts), heat dissipation, and duration of application of the RF current. Manipulation of these factors will allow for a more precise delivery of RF-generated heat to a target tissue while preserving the integrity of the skin.

There is a further need to discriminate various soft tissue structures by altering their relative absorption of electromagnetic radiation. More specifically, the preferential delivery of thermal energy to a soft tissue will allow a variety of applications from ablation to thermal conduction. By altering the extra-cellular fluid content of a soft tissue in specific ways, the delivery of thermal energy to a target tissue is achieved with minimal damage to skin and adjacent soft tissue structures.

## SUMMARY OF THE INVENTION

Accordingly, an object of the invention is to provide a method for tightening skin by the use of RF or other energy sources, including ultrasound, to promote a thermal conduction rather than ablation of collagen containing tissue.

Another object of the invention is to provide a method for tightening skin using multiple port focusing separately or combined with other energy sources

A further object of the invention is to provide a method for tightening skin through the management of conduction/convection energy losses in the soft tissue system.

Still a further object of the invention is to provide a method for tightening skin by altering tissue impedance achieved through surface hydration to increase conductance, injection of conducting and resisting





NSDOCID: <WO_____9805380A1_I_>

Skin resection procedures are limited in their application due to inherent scars. With face-lift procedures, scars can be hidden around the contour of the ear, thus providing an acceptable trade-off between the surgical scar and the aesthetic improvement. Surgical resection of skin on the hips, thighs, arms, knees and legs, however, provides only a modest improvement with fairly unsightly scarring. In addition, patients must undergo a post-operative phase of healing that may be both painful and inconvenient. Other risk factors, such as bleeding and infection, may prolong healing.

Liposuction is effective at removing fat in some areas, however it does not tighten the skin envelope. Skin resurfacing techniques that secondarily tighten excess skin (such as laser and chemical peels) employ a "standard thermal gradient" that requires burning off the superficial skin as a second degree burn. The thermal effects of collagen contraction in the deeper dermis occur, but require a painful healing phase due to the second degree burn. These modalities depend upon re-epithelialization with cell migration from the skin appendages. This process of re-epithelialization is similar to the healing of any thermal burn and is more likely to cause pigmentary irregularities due to the destruction of melanocytes in the epidermis.

A need exists for the use of radio frequency (RF) energy to achieve a reverse thermal gradient, controlled contraction of collagen containing tissue and the tightening of skin. With RF energy, a high frequency alternating current (usually 100,000 to 500,000 Hz) flows from a parallel series of electrodes into tissue. Ionic agitation is produced in the tissue around the electrode as the ions attempt to follow the changes of direction of the alternating current. This agitation results in frictional heating so that the tissue, rather than the electrode itself, is the primary source of





BNSDOCID: <WO_____9805380A1_I_>

fluids, invoking the inflammatory stage of the wound healing sequence to increase conduction and/or manipulation of collagen deposition and maturation.

Another object of the present invention is to provide a method for tightening skin by decreasing the shrinkage temperature of collagen by chemically altering molecular and fiber stability.

Yet another object of the present invention is to provide a method for tightening skin by modifying the thermal insulation characteristics of the skin to be more of a thermal conductor.

These and other objects of the invention are achieved in a method for tightening skin. An electromagnetic energy delivery device, with an energy delivery surface, is positioned with at least a portion of the energy delivery surface on a skin surface. Electromagnetic energy is delivered from the energy delivery surface through the skin surface, through the skin and to an underlying collagen containing tissue. An impedance of at least a portion of the skin or the underlying collagen containing tissue is modified. At least a portion of the collagen containing tissue is contracted and the surface of the skin is tightened.

In another embodiment, a thermal conductivity of the skin is modified to achieve skin tightening.

## BRIEF DESCRIPTION OF THE FIGURES

Fig. 1 is a perspective view of an apparatus for applying electromagnetic energy through the skin in order to cause a partial denaturization of collagen tissue, resulting in a tightening of the skin.

Figure 2 is a cross-sectional view of the skin and underlying tissue.

Figure 3 is a schematic representation of the collagen network.

Fig. 4 is a schematic diagram of an apparatus for applying electromagnetic energy to underlying subcutaneous layers or deeper soft tissue layers to create a desired contour effect by partially denaturing collagen tissue,





ISDOCID: <WO_____9805380A1_I_>

and without substantially modifying melanocytes and other epithelial cells in the epidermis.

Figure 5 is a block diagram of an RF system which can be utilized with the present invention.

Figure 6 is a block diagram of processing circuit of one embodiment of the invention.

## DETAILED DESCRIPTION

For purposes of this disclosure, the following definitions apply:

| | |
|---|---|
| Pre-Existing or Native Collagen | The protein substance of the white fibers (collagenous fibers) of skin, tendon, one, cartilage, and all other connective tissue. |
| Thermal Induction of Scar Collagen Deposition | A non-ablative neosynthetic process of collagen deposition as a reaction to inflammation induced by thermal injury. The resulting collagen is frequently referred to as nascent, as opposed to pre-existing. |
| Standard Thermal Gradient | The thermal content of soft tissue that is greater on the skin surface. |
| Reverse Thermal Gradient | A non-ablative remodeling effect upon either pre-existing or nascent scar collagen. |





BNSDOCID: <WO_____9805380A1_I_>

| | |
|---|---|
| Reverse Gradient of Collagen Contraction | A tissue environment in which collagen is preferentially contracted within a target tissue regardless of its relationship to adjacent or surface structures. |
| Contraction of Collagen | Morphological change that is produced by the cellular or molecular contraction of collagen-containing tissues. |
| Tissue Impedance (TI) | The resistance in tissue to the flow of energy or current. |
| Tissue Conductance | The transmission of energy or current through tissue. |
| Convection | The transfer of heat from one place to another by the movement of heated particles of gas or liquid. |
| Conduction | Process by which heat is transferred through matter, without transfer of the matter itself. |
| Fibroblast | The connective tissue cell that produces collagen and is the source of cellular contraction. |
| Radiofrequency (RF) | |





ISDOCID: <WO_____9805380A1_I_>

| | |
|---|---|
| Energy | The segment of the electromagnetic spectrum (wavelengths $10^{-3}$ to $10^{5}$ meters) that is released as thermal energy in tissue when ions are agitated by a high frequency alternating current. |
| Current Density | The amount of current in tissue per square area. |
| Ultrasound | The use of high frequency sonic energy that is released as thermal energy in tissue due to the agitation of component ions. |
| Cellular Contraction | The morphological change of collagen containing tissue that is due to the contractile properties of the fibroblast. |
| Molecular Contraction | An extracellular process that is due to the non-ablative denaturization of the collagen molecule. |

The present invention provides for the thermal shrinkage, or tightening of skin without the destruction of the overlying epidermis. Skin tightening with a reverse thermal gradient (hereafter "RTG") contraction of collagen can correct areas such as the thighs, knees, arms, back and hips without unsightly scarring of standard techniques. Areas previously corrected by surgical procedures, such as face and neck lifts, could also be corrected without requiring surgery or the typical incisions around the ear. Elastosis, or stretching of the abdominal skin from





BNSDOCID: <WO_____9805380A1_I_>

pregnancy, could be corrected without the long scar commonly associated with an abdominoplasty. Breast uplifts (mastopexies) would no longer require extensive incisions. It is believed that RTG contraction of collagen could be an effective, non-invasive alternative for the aesthetic treatment of these areas. RTG contraction of collagen could also be employed in areas not effectively treated by standard surgical techniques. Treatment of "cellulite" of the thighs and hips is one example.

Overall, the achievement of a RTG is the selective non-ablative contraction of collagen without thermal damage to surface and adjacent conducting tissues. Various modalities are available, (i) RF or other energy sources (ultrasound) that promote thermal conduction rather than ablation, (ii) multiple port focusing separately or combined with other energy sources, (iii) management of conduction/convection energy losses in the soft tissue system, (iv) alterations of tissue impedance (physical manipulation, surface hydration to increase conductance, injection of conducting and resisting fluids, invoking the inflammatory stage of the wound healing sequence to increase conduction, manipulation of collagen deposition and maturation, (v) decreasing the shrinkage temperature (Ts) of collagen by chemically altering molecular and fiber stability, and/or providing a mechanism to make the skin more of a thermal conductor than a thermal insulator.

Firming of soft tissue, such as the subcutaneous fat layer of the thighs, hips and breasts, with thermal induction of scar collagen deposition would provide a significant aesthetic benefit to patients by increasing the consistency of the soft tissue. Along with tightening of skin, the contour and consistency of subcutaneous tissue is enhanced without recourse to surgical procedures. As the device used does not require surgery, the method is more of an aesthetic treatment, rather than





ISDOCID: <WO_____9805380A1_I_>

an invasive operation. Other physicians (i.e. dermatologist or plastic surgeon) would initially administer treatments. Eventually, aestheticians could potentially be certified to administer these treatments, thereby greatly increasing access of their clients to this technology. Expansion of the marketplace into health spas as a franchise is certainly a possibility with these methods and medical devices.

Typically, the subcutaneous fat layers have loculations from fibrous septae that contain collagen. These fibrous septae can be contracted to tighten the soft tissue in areas such as the hips and thighs. Along with these extracellular effects of collagen, intracellular effects upon the fat cell, or lipocyte, by thermal induction will cause a net reduction of fat from the lipocyte which will achieve a net reduction in volume of the treated area. A second device (such as ultrasound focused at the appropriate level on the subcutaneous tissue) may be used in tandem with the RTG (RF device) heating pad to achieve liposculpture of the treated area.

A second broad application of RTG contraction of collagen involves the induction of scar collagen deposition. Thermal induction can incite the wound healing sequence of fibroblast proliferation with nascent scar deposition in soft tissues normally devoid or deficient of collagen. By introducing a carefully controlled thermal injury to structures that do not contain pre-existing collagen, it is possible to create scar collagen that can then be remodeled or contracted by subsequent treatments.

Another application of RTG is the treatment of sleep apnea, in which the soft palate in the back of the throat collapses and interferes with or obstructs breathing in sleeping individuals. Current treatments involve the surgical shortening of this structure, or laser treatments which employ a standard thermal gradient which burns the mucosa. The soft palate





BNSDOCID: <WO_____9805380A1_I_>

contains a minimal amount of collagen. Thermal induction of scar collagen deposition on the soft palate followed by contraction to shorten the palate could relieve the functional airway obstruction. Furthermore, burning of the mucosa is avoided by employing a RTG instead of a standard thermal gradient.

Additional medical applications of RTG contraction of collagen could include the treatment of unstable joints due to collateral ligament laxity. The thermal induction and deposition of scar collagen with subsequent contraction will reduce the hypermobility of these joints. In a similar fashion, this technology can be applied in the treatment of unstable spinal column disorders, such as lumbar or cervical compression syndromes, and scoliosis that is often encountered in younger women. In this application, thermal induction of scar collagen deposition would be initiated in precise locations along the spine. Additional treatments would then contract the scar collagen to counter the vectors of spinal deviation and increase the stability of the spine. In addition, the thermal induction of osteoblasts in the periosteum will result in callus (calcium matrix) formation. As callus contains a higher percentage of collagen than mature bone, subsequent remodeling with thermal contraction is possible. Maturation of the remodeled callus with calcium matrix deposition will result in a stable bony fusion of treated areas.

Weaknesses of the abdominal wall, such as hernia or diastases rectus, could also be managed with the deposition of scar collagen that is subsequently contracted. Treatment of urinary incontinence and bladder prolapse in women could be treated effectively with a device inserted into the vagina that would induce scar collagen deposition and contraction with RTG. Treatment of gastroesophageal reflux disease could be accomplished in a similar fashion with a device introduced





ISDOCID: <WO_____9805380A1_I_>

endoscopically. Aging of the skin involves thinning of the dermal layer from the progressive loss of collagen matrix. As a consequence, there is a reduction in the skin's turgor. Wrinkling of the skin occurs as a consequence of inadequate support of the epidermis. Therefore, treatment of wrinkles could be accomplished by combining a RTG contraction of dermal collagen with the induction of scar collagen deposition. Improved skin turgor is accomplished by first replenishing the collagen matrix that has been lost with aging. Following the induction and deposition of nascent scar collagen in the dermis, contraction of collagen with a RTG would correct wrinkling of the skin without resorting to "resurfacing" techniques that require the application of a standard thermal gradient burn to the skin. Prolonged healing and pigmentary irregularities would be avoided. The superficial papillary dermis is the treatment zone for this application.

A derivation of Ohm's law provides a means to alter and discriminate the biophysical properties of soft tissue. For electrical systems, $I = E/R$, where I is intensity of the current (measured in amperes), E is the energy potential (measured in volts), and R is the resistance (measured in ohms). For soft tissue systems, the current density delivered to a soft tissue target is inversely related to tissue impedance (TI). Most biological systems function as a combination of series and parallel circuits. If the tissue behaves as a series system, release of heat will occur in higher resistance target tissue. For electrical systems that function in parallel, delivery of current and energy may be shunted to low resistance areas.

Consequently, a higher power setting may be required for thermal release in this tissue system as higher resistance areas are bypassed. In these systems, high resistance areas may be protected and thermal effects





BNSDOCID: <WO_____9805380A1_I_>

may occur in tissue in which impedance is lower and current density is higher. Skin contraction applications will typically function in series, while deeper tissue applications may behave as a parallel system. Paradoxical effects may be observed depending upon the electrical behavior of the system.

Modulation of RF frequency (FM) may provide additional delineation of the impedance characteristics of tissues. More specifically, an increase in the frequency may correlate to a greater thermal release in higher impedance tissues. In a "series" system, an increase in RF frequency will equate to an increase in the thermal content of target tissues that are resistors. In a parallel system, target tissues may be configured differently to augment current density in a low impedance environment. Different frequency parameters may be required.

Raising the extracellular fluid (ECF) content of soft tissue results in a reduction in tissue impedance, which increases current density and thermal delivery to target tissues that have a relatively higher impedance. Target tissues can also be physically manipulated to lower ECF content and further raise their local tissue impedance as resistors. The thermal energy released at a target tissue is expressed as joules, or the heat dissipated in an electrical system. The thermal energy released at the target tissue is directly related to the tissue impedance and is exponentially related to the current density.

An understanding of tissue impedance in reference to the different phases of the wound healing sequence is critical in predicting thermal remodeling effects upon collagen. In general, conductors such as inflammatory edema or normal saline will increase the extracellular fluid. Transfer of RF energy through tissue without thermal release is facilitated. Injection of glucose containing solutions or conditions that





SDOCID: <WO_____9805380A1_I_>

reduce the ECF will act as resistors that will target tissue for thermal release and the remodeling of collagen.

The following is a tissue impedance scale:

Conductors

<----------

---------->

Resistors

Saline..... Edema..... Immature/..... Mature.....

Glucose..... Native

Fibroplasia Scar Collagen

Collagen

If the wound healing sequence is examined, the initial stage involves the creation of inflammatory edema that raises ECF and conductance. Following a lag period of three to five days, the second phase of fibroplasia involves the multiplication and migration of fibroblasts to the wound. The deposition of scar collagen will increase tissue impedance even though (ECF) ground substance content is high. The final phase of scar collagen maturation begins at two weeks and continues for several weeks. During this phase, the collagen becomes progressively more insoluble due to the loss of ground substance with a concomitant increase in intermolecular and interfiber cross linkage. Concurrent with this change is a gradual increase in tissue impedance. Preexisting or native collagen is even more insoluble and will exhibit the highest tissue impedance.

The ability of energy to do work in this soft tissue system corresponds to the contraction of collagen by the disruption of crosslinks





BNSDOCID: <WO_____9805380A1_I_>

in the triple helix of the molecule. An accurate measure of energy delivery to the tissue is required. Temperature is not a measure of heat content or energy delivery to tissue. Rather, it is a momentary snapshot of the energy level of the tissue. It is the delivery of energy over time as the heat content (joules/second) that is the most accurate measure of energy available for the contracture of collagen. Another factor that affects the heat content of tissue is the thermal dissipation that occurs through thermal conduction away from the target tissue and the thermal convection from vascular and surface structures.

Control of multiple factors is required to create the optimal RF tissue environment for the non-ablative contraction of collagen. Initially, heat is required as a precursor of the "RF effect. This may be supplied from a variety of sources, such as ultrasound. The thermal energy acts as an amplifier of the RF electrode rather than a direct agent to cleave the molecular crosslinks. This beginning thermal sequence provides the ionic agitation required for the magnetic induction by the RF electrode. The magnetocaloric effects predicts the thermal requirement for the magnetic induction of tissue and is described by $\Delta T/\Delta H = -T/C_H (\partial M/\partial T)_H$, where $\Delta T$= change in temperature, $\Delta H$ = change in magnetic field, and $C_H$ = Specific heat capacity/volume. The ionic polarization of the tissue by the RF electrode produces an alternating magnetic moment that cleaves the collagen crosslinks with an "in phase" alternating ionic motion. In other words, the magnetocaloric effect increases the induced magnetic moment within the tissue. Additional thermal energy beyond this effect will only damage tissue and should be avoided.

FM (frequency modulation) for each tissue system is crucial to achieving the most efficient reverse gradient for collagen contraction.





ISDOCID: <WO_____9805380A1_I_>

The appropriate frequency that is in phase with the most efficient ionic motion is provided as "work" to the system where P (watts or joules/second)=$I^2R$. Consequently, the tissue environment should be configured to increase current density by decreasing tissue impedance. Excessive heat production from "out of phase" frictional agitation is avoided while direct ionic cleavage of collagen crosslinks is facilitated. The net result is the contraction of collagen with lower power requirements which reduces thermal damage to the tissue.

There are several methods available to alter the tissue impedance of the skin surface and soft tissue to serve either as a conduit or as a target resistor. For example, current density can be increased with the injection of a conductor (decrease TI) such as normal saline, which allows the subcutaneous plane to act as a conduit to the target tissue. Conducting fluid that increases current density to the target tissue will increase thermal release in a logarithmic fashion. In addition to lowering tissue impedance and increasing current density, saline injection into target tissues enlarges the effective surface area of the RF electrode. A more uniform inductive effect is provided by the saline tissue interface. Increasing the TI of adjacent structures by stretching skin over rollers (decreasing ECF) will have a similar effect by funneling the current to the conduit tissue. Injection of a resistor fluid, such as glucose, into a target tissue will increase the TI and thermal release in a linear fashion. Current density of conduit tissues and thermal release at target tissues is greatly enhanced by combining the injection of conducting (saline) and resisting (glucose) fluids. In other words, soft tissue injection functions as a tissue impedance "lens" that focuses thermal energy in target tissues while reducing collateral damage to adjacent structures. This approach is mainly used for deeper soft tissue applications. In general, the





BNSDOCID: <WO_____9805380A1_I_>

manipulation of the impedance characteristics of target tissues with either conductors or resistors will create the optimal RF environment that has the appropriate amount of heat and current density for the magnetic induction of that tissue.

For skin applications, an understanding of dermal impedance is required. Reduction in the thermal load at the skin entry port subjacent to the RF electrode may be accomplished by reducing the tissue impedance of the skin with hydration, i.e. a hydrogel applied under the electrode strip is used to increase ECF and conductivity of the skin entry point. A more selective (time-dependent) hydration of the epidermis and papillary dermis under the electrode will conduct current through the superficial skin and target the deeper dermis as a resistor. This pre-determined period of hydration is selected for the specific dermal level of the target tissue. The target tissue interface is positioned between the overlying hydrated conducting skin and the subjacent non-hydrated dermis that acts as a resistor. A RTG for dermal and subdermal contraction of skin is achieved when the current is released as thermal energy in the deeper dermal tissue. More specifically, hydration of the skin is achieved by initially applying an anesthetic gel that has an aqueous penetrant formulation. The treatment area is then submerged in a bath for a variable period of time, as dictated by the dermal target level. This specific methodology would have cutaneous applications for scar collagen deposition and contraction to correct wrinkling and aging of the skin. Wrinkling of the skin is treated by targeting a more superficial dermal level and is achieved by reducing the duration and depth of skin hydration. Deeper dermal effects for skin contraction would be achieved by longer periods of skin hydration. In addition, the deeper dermal and subdermal target tissues can be discriminated further from the conducting





ISDOCID: <WO_____9805380A1_I_>

superficial skin with the injection of a fluid resistor such as glucose. Heating of the glucose prior to injection in the target tissue may additionally serve to lower the RF power requirement for contraction of collagen. The "tumescent" technique used for liposuction could be used as a familiar technique of injection.

Another approach to alter TI is to invoke the inflammatory stage of the wound healing sequence. Similar to the induction of scar collagen deposition, the wound healing sequence can be initiated to alter the TI and current density of soft tissue. The initial inflammatory stage of the wound healing sequence involves creation of edema fluid within the extracellular spaces. The ECF will be increased as edema fluid and will allow tissue to act as a conductor/conduit. This fluid is a conductor whose osmolarity is similar to normal saline and is formed by the extravasation of serum from the capillary bed or post capillary venules. Changes in endothelial permeability as mediated by histamine and bradykinin will appear morphologically as erythema of the skin. Various modalities are available to incite this inflammatory phase. The topical application of mechanical, thermal, chemical or pharmacological agents to induce cutaneous inflammatory edema will allow current to be conducted through the skin without thermal damage. Retin A, alpha hydroxy acids, and dilute TCA may be applied to lower surface impedance and thermal damage at the skin entry point.

In addition, the stability of the triple helix can be chemically altered prior to thermal denaturization. The collagen shrinkage temperature (Ts) is an indication of molecular stability as is determined by the amount of crosslinkage. Ground substance such as chondroitin sulfuric acid (CSA) increases molecular stability by promoting salt-like crosslinks between collagen fibers. Reagents such as hyaluronidase





3NSDOCID: <WO_____9805380A1_I_>

(Wydase) that enzymatically remove CSA will reduce fiber stability and the shrinkage temperature (Ts). Typically, a reduction of 10 °C in the Ts is obtained by the injection of this reagent. As a result, power requirements and thermal damage to conducting and target tissues would be reduced. Wydase may be combined with a resistor fluid such as glucose to augment thermal release while lowering the temperature required for contraction. Typically, the solution would be combined with a dilute local anesthetic and injected into target tissues with the "tumescent" technique.

Pharmacological methods to alter the solubility of collagen may also be an effective way to alter the relative conductance and resistance of soft tissue. Anti-inflammatory medications such as steroids will reduce conductance and edema fluid of target tissues. Other agents such as vitamin E will also reduce conductance by promoting the scar maturation process. During this process, the decrease in collagen solubility is due to loss of ground substance and an increase in molecular cross linkage. Reversing the maturation process involves increasing the solubility of collagen with various lathrogenic agents (such as beta aminoproprionitrile, d-penacillinamine and colchicine). Cross linkage is retarded and the tissue will exhibit a higher conductance due to the increase in ground substance. These various pharmacologic agents can be administered either topically, systemically or by direct injection.

In contrast to the application of energy, manipulation of energy losses in the system provides another means to achieve the contraction of collagen without surface ablation. Thermal conduction losses occur through the passive dissipation of heat through tissue and is limited by local tissue parameters. In contrast, convection transfer of heat occurs through the physical movement of heated matter away from the target





SDOCID: <WO_____9805380A1_I_>

tissue and is a process that can be actively manipulated. Flash cycles of surface cooling interspersed with heating will allow greater heat dissipation at the surface than the underlying dermal tissue. Sequential cycles of surface cooling and tissue heating provide a RTG as the heat dissipated from surface convection occurs faster than subdermal conductive losses. A progressive increase in the subdermal heat content occurs while maintaining a constant surface temperature.

Promoting energy losses with surface convection cooling is a necessary adjunct to contracting collagen without collateral thermal damage from excessive ionic friction and agitation. A surface convection cooling pad should cool tissues but provide enough thermal energy required by the magnetocaloric effect for the magnetic induction and cleavage of molecular collagen crosslinks.

Other approaches to reduce the thermal load to the skin surface can be employed. Dispersion of current density over a larger surface area will reduce the thermal load to the skin surface. Multiple port focusing with RF and ultrasound in a tandem fashion will have a similar effect of dispersing energy. Between the electrode strips, a non-conductive medium can be used to directly preheat the dermal and subdermal target tissues. A combination of these modalities can be employed to avoid thermal damage to the skin surface.

Additional device modalities are available to physically manipulate tissue and decrease ECF, i.e. the manipulated tissue behaves like a resistor. These devices may be applied in tandem or as part of the RF electrode. They include rollers, suction cups or a combination of both. Simple mechanical trauma such as rolling the skin will initially increase the TI, but may subsequently augment conductance of the skin with the formation of inflammatory edema at the current entry area of skin under





BNSDOCID: <WO_____9805380A1_I_>

the electrode. As a more efficient conductor of current, the skin surface will avoid thermal damage and allow more efficient delivery of energy to target tissues. Target tissues will also respond in a similar fashion with the formation of inflammatory extracellular fluid. Although an initial drop in TI will be observed, the solubility and conductance will decrease with the deposition of scar collagen within 72 hours after initial injury. Subsequent treatment may be timed to take advantage of the increasing resistance of the target tissue to provide a greater release of thermal energy. Additional scar maturation with increased cross linkage may make the collagen more susceptible to contraction from both a TI and a chemical bonding perspective, even though the shrinkage temperature (Ts) is raised. In general, collagen maturation with additional cross-linkage will increase the potential for contraction. Mature or native collagen should exhibit a greater thermal release (TI increase) and molecular contraction than more soluble and immature scar collagen.

A cross indexing of these approaches should reveal an appropriate combination of methods for each clinical application. Monopolar and bipolar patterns of current density in combination with these methods that alter tissue conductance will allow greater latitude in shaping the specific pattern of RF energy delivery.

The present invention involves application of a RTG to heat the underlying dermal collagen, while protecting the superficial epidermal skin. The device used to achieve this effect is similar to a heating pad. It employs radio frequency (RF) energy that is precisely focused on the underlying dermal collagen of treatment areas.

In addition, this energy source can be employed in tandem with other energy sources. Ultrasound can be used as a non-inductive source can provide the initial energy of ionic agitation required for the magnetic





SDOCID: <WO_____9805380A1_I_>

RF induction of collagen containing tissue. By changing the local TI with physical and pharmacological manipulation of the skin and target tissues, a more accurate delivery of thermal energy is achieved. Partial denaturization of collagen is achieved with each application and the use of sequential treatments will allow for more precision of the end result.

Depending upon the topography of a treatment area, the heating pad is designed to provide the appropriate vectors of contraction. Areas of application are not confined by requirements to hide surgical incisions or to transition chemical peels or laser resurfacing into aesthetic boundaries. And since scarring and pigmentary irregularities are avoided, skin tightening can now occur in areas previously considered "off-limits" to standard methods of correction.

The medical devices and procedures that are designed specifically for skin contraction will have the following components: initially, the skin is hydrated to a specific dermal level before the RF heating pad is applied. This allows conductance of RF energy through the skin without thermal release. The subjacent dermis which has not been hydrated will respond as a resistor with the release of thermal energy to contract or induce collagen. In addition, ultrasound transducers are incorporated with mechanical rollers that are applied as a separate device over the RF heating pad. The rollers manipulate tissue impedance and the ultrasound transducers are aligned as parallel opposing ports that are focused with an overlapping energy pattern at the target dermal level. By simultaneously heating the target tissue with ultrasound, power requirements are reduced for the RF heating pad.

The initial evaluation is begun with a digitized image of the patient Each potential treatment area is captured for analysis. A cursor is used to determine the appropriate boundary of each treatment area for either a





BNSDOCID: <WO_____9805380A1_I_>

minimally invasive or non-invasive approach. For non-invasive skin contraction or soft tissue remodeling, a vector analysis is performed to orient the parallel electrode array on the patient's skin. For the minimally invasive contraction of skin and soft tissue, an intraoperative infrared image is captured and referenced to the preoperative digital evaluation. During the procedure, the peak infrared emission pattern for each area is captured and digitally incorporated into an entire mosaic of the treatment area. This peak emission mosaic is compared to the preoperative digital evaluation for the position, boundary and appropriate vectors of contraction in addition to the recommended infrared emission levels. With this method of preoperative and intraoperative analysis, an accurate depiction of the post operative result can be provided to the patient during the initial preoperative evaluation.

Taking into consideration many of the methodologies that have been discussed to achieve a RTG contraction of collagen, the following provides a sample application sequence. A treatment sequence for clients desiring skin contraction involves a variety of modalities.

For one week prior to treatment, a topical agent such as Retin A or alpha hydroxy acid is applied to the skin to produce an inflammatory edema. Conductance of RF energy through the superficial skin will be facilitated. The client begins her treatment session with the application of an aqueous penetrant gel which contains a concentrated local anesthetic. The gel is massaged into the specifically marked treatment areas for 30 minutes. These areas are preferentially hydrated by having the client bathe for approximately one hour with water temperature approximately 100° F. Actual bathing time will vary depending upon the treatment level within the skin. Additional preparation of the treatment area may require injection of impedance altering fluids such as saline (conductor) or





\SDOCID: <WO_____9805380A1_I_>

glucose (resistor). This solution may be combined with Wydase and xylocaine to lower power requirements and provide anesthesia. The solution is injected with the "tumescent" technique. This technique, typically used for deeper soft tissue applications, may be employed for skin contraction. The next stage of the treatment sequence involves the application of the RF heating pad that has been specifically configured from the treatment area. Incorporated into the RF heating pad is a cooling channel that will cycle dermal heating and surface convection cooling. A second device that employs mechanical rollers and ultrasound transducers to focus additional thermal energy in the skin may also be used. Multiple treatments of this non-invasive program provides for greater precision of the end result while avoiding blistering of the skin. In addition, periodic maintenance treatments will be required to counter the continuation of the aging process.

Minimally invasive techniques are possible that involve the percutaneous insertion of a medical device through the skin that can achieve a RTG for the contraction of skin. The device can be used in tandem with an endoscope to provide hemostasis and aid the dissection of the subcutaneous plane. The device consists of a multiple purpose canula that is used for subcutaneous dissection and liposuction in addition to collagen contraction. In one embodiment, a spatula shaped canula has a light source on the dorsal surface which trans illuminates the skin and creates a focused light pattern on the skin to determine depth and uniformity of the subcutaneous plane of dissection. A liposuction portal is placed on the ventral aspect of the device and allows aesthetic modification of the subcutaneous fat. A separate energy source is also mounted on the dorsal aspect of the canula and is used to "paint" the subdermal and dermal tissues for the contraction of collagen. This device





BNSDOCID: <WO_____9805380A1_I_>

may either be a separate canula with the transilluminator or combined as a single combined device with the subcutaneous dissection/suction canula. Typically an RF electrode is utilized as the primary energy source. Other energy sources may include an ultrasound transducer or a coherent $CO_2$ light source with a diffuser.

For example, a facelift procedure would typically involve the initial injection of a tumescent solution that contains a dilute xylocaine/epinephrine mixture with added Wydase. Anesthesia and vasoconstriction with lowering of the collagen shrinkage temperature (Ts) is provided with this solution. Through small 1 cm preauricular and submental incisions, the subcutaneous dissection/ liposuction canula is inserted. Through a separate 1 cm incision, an endoscope may be inserted for direct visualization and hemostasis. After development of a uniform superficial subcutaneous plane of dissection, liposculpture of the underlying subcutaneous tissue is achieved. With a separate or combined canula, skin contraction is achieved in a uniform fashion by sweeping the energy source in the superficial subdermal plane of dissection. Accurate surface and depth orientation is provided by the transillumination pattern of the skin.

Another example of a minimally invasive procedure is the correction of the post partum ptosis of the breast. Typically, large anchor shaped incisions are employed to achieve a mastopexy or breast uplift. In contrast, uplifting and tightening of the breast envelope can be achieved through small periareolar incisions with the minimally invasive methodology of The present invention. Achievement of a three-dimensional enhancement rather than a two-dimensional uplifting is provided by preoperatively determining the appropriate vectors of contraction with digital capture software, i.e. a radial pattern of sweeping





ISDOCID: <WO_____9805380A1_I_>

will result in a longitudinal shortening of the breast envelope, whereas a circular sweeping pattern around the circumference of the breast will increase projection by tightening the base perimeter dimension. With this approach, a variety of esthetic procedures is also possible for the abdomen, thighs and arms.

The present invention provides the esthetic surgeon with the opportunity to achieve a more immediate result in a minimally invasive fashion. The larger incisions of typical esthetic procedures is eliminated. Contour irregularities and skin looseness that is typical of suction lipectomy procedures is avoided.

The same concepts of altering tissue impedance (TI) for collagen contraction can be applied for tissue ablation. Although higher power levels are required, effective radiation doses for tumor ablation can be reduced by potentiating energy release at target tissues through the manipulation of tissue impedance. As a direct benefit, the collateral damage to normal adjacent structures would be minimized.

Power requirements for cancer management can be reduced further by altering intracellular metabolism rather than ablating tumor cells. If remission or homeostasis is defined as a state in which net tumor growth has ceased, then the creation of a state can be achieved by increasing cell death (ablation) or decreasing cell growth by suppression of mitosis with intracellular thermal induction. Most oncologic treatment modalities focus upon various ablation strategies that place little emphasis on reducing mitotic activity. Suppression of cancer cell mitosis with intracellular thermal induction has significant potential in reestablishing homeostasis at lower power requirements. The patient care algorithm would consist of a continuing sequence of treatments to maintain the balance between cell death and cell growth while eliminating damage to





BNSDOCID: <WO_____9805380A1_I_>

adjacent tissue. The thermal induction of homeostasis will also provide a continuing opportunity for a competent immune response by the patient. A balance between ablation and thermal induction of homeostasis is also promoted by selectively altering the tissue impedance of target and conducting tissues. Power or dose requirements for ablation can be further reduced by modifying the cellular kinetics of the tumor. Thermal induction will place cells in phase during the mitotic cycle, rendering the tumor more susceptible to ablation. Cycles of treatment with thermal induction will stagger phases of cell multiplication to predictable periods that can be timed with the patient's oncologic treatment (i.e. chemotherapy and/or radiation therapy). By increasing the specificity of thermal ablation, sequential management of metastatic disease may be possible.

Thermal ablation of normal tissue can be used for aesthetic liposculpture. By altering TI and conductance with these methods, ablation of subcutaneous fat can be achieved with a greater degree of precision. The current use of "tumescent" injection of an impedance altering solution integrates easily with the present invention.

Non-ablative thermal modification of intracellular metabolism is another potential application with this technology. If a low grade injury pattern is sustained during exercise, thermal injury should incite the same sequence of extracellular and intracellular inflammation that leads to hypertrophy of a muscle cell. This method can be applied for disuse atrophy of muscle in patients who are paraplegic or who are in catabolic stress for any reason. Disuse atrophy sustained in zero gravity environments may be avoided with intracellular thermal induction of muscle.

It may also be possible to modulate the synthesis of collagen by the fibroblast with a combination of both intracellular and extracellular





ISDOCID: <WO_____9805380A1_I_>

thermal induction. The thermal inductive effects should be different for intracellular suppression of collagen synthesis than scar collagen formation as provided by the wound healing sequence. A direct application of intracellular thermal suppression of collagen synthesis and fibroblast mitosis is the reduction of hypertrophic scarring in surgical incisions.

Bony callus formation and formation by the osteoblast may also be modulated by the selective balance between intracellular and extracellular thermal inductive effects.

Alternately, the healing by regeneration instead of scarring may be influenced by the selective thermal induction of intracellular and extracellular processes. Regeneration of soft tissue structures may occur more readily in a conducting milieu than in an impedance environment which would promote the deposition of scar collagen. Peripheral nerve regeneration should be aided by selectively suppressing scar formation at the proximal stump of a transacted nerve, and the demyelination of nerve fibers could be prevented with this modality. Determining the impedance/conductance conditions and electromagnetic field pattern of fetal development should provide necessary information to promote healing by regeneration. The intracellular degeneration and cell membrane dissolution of the cerebral cortex may be prevented by maintaining the appropriate magnetic field around these structures.

## Definitions of Standard Gradients





3NSDOCID: <WO_____9805380A1_I_>

**A Standard Thermal Gradient** is the application of electromagnetic energy. The soft tissue without modification of surface angle incidents or tissue parameters that change energy transmission and release in that tissue.

**A Standard Gradient of Molecular Collagen Contraction and Cellular Contraction of Collagen Containing Tissue** is the contraction of that tissue without modification of surface energy angle incidents or tissue parameters that change energy transmission and release within that tissue.

**A Standard Gradient of Energy Delivery** is the delivery of energy into tissue without modification of surface incidents or tissue parameters that change energy transmission and release within that tissue.

**A Standard Gradient of Tissue Interaction** is the interaction of tissue with energy without modification of surface angle incidents or tissue parameters that would change the pattern of tissue interaction with energy.

## Definitions of Reverse Gradients

**A Reverse Thermal Gradient** is defined by its relationship to a Standard Thermal Gradient.

**A Reverse Thermal Gradient** is cooler on the surface or in adjacent tissues when compared to a Standard Thermal Gradient that has a target tissue with the same heat content.

**A Reverse Thermal Gradient** can also be expressed as:

1. A reduced Standard Thermal Gradient between the surface and underlying tissue, or between adjacent and target tissues.





SDOCID: <WO_____9805380A1_I_>

2. An Equalized Thermal Gradient between the surface and underlying tissue, or between adjacent and target tissues.

3. A Thermal Gradient in which ablation does not occur on the surface or in adjacent tissue (next to a target).

4. A Thermal Gradient in which ablation is reduced on the surface or adjacent tissue in comparison to a Standard Thermal Gradient.

**A Reverse Gradient of Molecular Collagen Contraction and Cellular Contraction of Collagen Containing Tissues** is defined by its relationship to a Standard Gradient Contraction of Collagen Containing Tissues.

**A Reverse Gradient of Collagen Contraction** results in the preferential contraction of a target tissue that is greater in comparison to a Standard Gradient of Collagen Contraction of target and surface/adjacent tissues.

**A Reverse Gradient of Collagen Contraction** can also be expressed as:

1. A Reduced Standard Gradient of Collagen Contraction between surface and underlying tissue or between adjacent and target tissues.

2. As an Equalized Gradient of Collagen Contraction between the surface and underlying tissue or between adjacent and target tissues.

3. A Gradient of Collagen Contraction in which ablation does not occur in surface or adjacent tissues.





BNSDOCID: <WO_____9805380A1_I_>

4. A Gradient of Collagen Contraction in which ablation is reduced on the surface or adjacent tissues in comparison to a Standard Gradient of Collagen Contraction.

**A Reverse, Gradient of Energy Delivery** is defined by its relationship to a Standard Gradient of energy delivery.

**A Reverse Gradient of Energy Delivery** is the preferential delivery of energy to a target tissue that is greater in comparison to a Standard of Gradient of energy delivery regardless of the energy content of surface and adjacent tissues.

**A Reverse Gradient of Energy Delivery** can also be expressed as:

1. A Reduced Standard Gradient of Energy delivery between surface and underlying tissue or between adjacent or target tissues.

2. An Equalized Gradient of Energy delivery between the surface and underlying tissue or between adjacent and target tissues.

3. A Gradient of Energy delivery in which ablation does not occur on surface or in adjacent tissues.

4. A Gradient of Energy delivery in which ablation is reduced on surface or adjacent tissues in comparison to a Standard Gradient of energy delivery.

**Reverse Gradient of Tissue Interaction** is defined by its relationship to a Standard Gradient of tissue interaction.





ISDOCID: <WO_____9805380A1_I_>

**A Reverse Gradient of Tissue Interaction** is the achievement of a desired soft tissue effect on a target tissue with a reduced soft tissue effect to surface or adjacent structures in comparison to a Standard Gradient of interaction.

**A Reverse Gradient of Tissue Interaction** can also be expressed as:

1. A Reduced Standard Gradient of tissue interaction between surface and underlying target tissue or between adjacent and target tissues.

2. An Equalized Gradient of tissue interaction between the surface and underlying target tissue or between adjacent and target tissues.

3. A Gradient of tissue interaction in which ablation does not occur on surface or in adjacent tissues next to a target tissue.

4. A Gradient of tissue interaction in which ablation is reduced on surface or adjacent tissues next to a target tissue in comparison to a Standard Gradient of tissue interaction.

## Claims of Electromagnetic Energy and Aesthetic Enhancement

1. The Use of Electromagnetic Energy to Achieve a Reverse Gradient of Molecular Contraction of Collagen and a Reverse Gradient of Cellular Contraction in Collagen Containing Tissue without Ablation.





BNSDOCID: <WO_____9805380A1_I_>

2. The Use of Electromagnetic Energy to Achieve a Reverse Gradient of Molecular Contraction of Collagen and a Reverse Gradient of Cellular Contraction in Collagen Containing Tissue with reduced Ablation in comparison to a Standard Thermal Gradient.

3. The Use of Electromagnetic energy in Soft Tissue to Achieve a Reverse Gradient of Energy Delivery without ablation.

4. The Use of Electromagnetic Energy in Soft Tissue to Achieve a Reverse Gradient of Energy Delivery with Reduced Ablation in Comparison to a Standard Thermal Gradient.

5. The Use of Electromagnetic Energy in Soft Tissue to Achieve a Reverse Gradient of Energy Delivery with Ablation of Target Tissue but without Ablation of Surface or Adjacent Tissues.

6. The Use of Electromagnetic Energy in Soft Tissue to Achieve a Reverse Gradient of Energy Delivery with Ablation of Target Tissue but with reduced Ablation of Surface or Adjacent Tissues in Comparison to a Standard Thermal Gradient.

7. The Use of Electromagnetic Energy to Reconfigure the Surface and Contour of Soft Tissue with a Reverse Gradient of Energy Delivery.

8. The Use of Electromagnetic Energy to Reconfigure the Surface Contour of Soft Tissue with a Reverse Cellular and Extracellular Gradient of Energy Delivery.





NSDOCID: <WO_____9805380A1_I_>

9. The Use of Electromagnetic Energy to Reconfigure the Surface and Contour of Soft Tissue with a Reverse Cellular and Extracellular Gradient Contraction of Collagen Containing Tissues.

10. The Use of Reverse Gradient of Energy Delivery to Alter the Intracellular Metabolism of Soft Tissue (use different cell types as dependent claims; the adiposcyte, myocyte, fibroblast, fibrocyte, epidermal cell, melanocyte, osteoblast, osteocyte, neuron, skin adnexal cells - hair follicle, sebaceous gland, sweat gland).

11. The Use of a Reverse Gradient of Energy Delivery to Achieve Molecular Contraction of Collagen and Cellular Contraction of Collagen Containing Tissues.

12. The Use of a Reverse Gradient of Energy Delivery to Alter the Extracellular Metabolism of Soft Tissue.

**Dependent Claims of Electromagnetic Energy and Aesthetic Enhancement**

1. The Use of Electromagnetic Energy to Alter Soft Tissue Volume with a Reverse Gradient of Energy Delivery:

a. Without Ablation.

b. With Reduced Ablation in Comparison to a Standard Gradient.

c. With Ablation.





BNSDOCID: <WO_____9805380A1_I_>

2. The Use of Electromagnetic Energy to Alter Soft Tissue Consistency with a Reverse Gradient of Energy Delivery:

a. Without Ablation.

b. With Reduced Ablation in Comparison to a Standard Gradient.

c. With Ablation.

3. The Use of Electromagnetic Energy to Alter the Overall Function of a Soft Tissue Structure with a Reverse Gradient of Energy Delivery:

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient.

C. With Ablation.

4. The Use of a Reverse Gradient of Energy Delivery to Reconfigure the Surface and Contour of Soft Tissue by Altering the Intra-cellular Processes (metabolism), of Component Cells, i.e., the adiposcyte, myocyte, fibroblast, fibrocyte, epidermal cell, melanocyte, osteoblast, osteocyte, neuron, skin adnexal cells - hair follicle, sebaceous gland, sweat gland.

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Cells in a Target Area.





ISDOCID: <WO_____9805380A1_I_>

5. The Use of a Reverse Gradient of Energy Delivery to Change the Consistency of Soft Tissue by Altering the Intra-cellular Processes of Component Cells, i.e., the adiposcyte, myocyte, fibroblast, fibrocyte, epidermal cell, melanocyte, osteoblast, osteocyte, neuron, skin adnexal cells - hair follicle, sebaceous gland, sweat gland.

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Cells in a Target Area.

6. The Use of a Reverse Gradient of Energy Delivery to Change the Volume of Soft Tissue by Altering the Intra-cellular Processes of Component Cells, i.e., the adiposcyte, myocyte, fibroblast, fibrocyte, epidermal cell, melanocyte, osteoblast, osteocyte, neuron, skin adnexal cells - hair follicle, sebaceous gland, sweat gland.

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Cells in a Target Area.

7. The Use of a Reverse Gradient of Energy Delivery to Change the Overall Function of a Soft Tissue Structure by Altering the Intra-cellular Processes of Component Cells, i.e., the adiposcyte, myocyte, fibroblast, fibrocyte, epidermal cell, melanocyte, osteoblast, osteocyte, neuron, skin adnexal cells - hair follicle, sebaceous gland, sweat gland.

A. Without Ablation.





BNSDOCID: <WO_____9805380A1_I_>

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Cells in a Target Area.

8. The Use of a Reverse Gradient of Energy Delivery to Change the Growth of a Soft Tissue Structure by Altering the Intra-cellular Processes of Component Cells, i.e., the adiposcyte, myocyte, fibroblast, fibrocyte, epidermal cell, melanocyte, osteoblast, osteocyte, neuron. skin adnexal cells - hair follicle, sebaceous gland, sweat gland.

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Cells in a Target Area.

9. The Use of a Reverse Gradient of Energy Delivery to Change the Extracellular Metabolism of a Soft Tissue Structure.

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Extracellular Tissue in a Target Area.

10. The Use of a Reverse Gradient of Energy Delivery to Reconfigure the Surface and Contour of Soft Tissue by Altering the Extracellular Metabolism of that Tissue.

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Extracellular Tissue in a Target Area.





ISDOCID: <WO_____9805380A1_I_>

11. The Use of a Reverse Gradient of Energy Delivery to Change the Volume of Soft Tissue by Altering the Extracellular Metabolism of that Tissue.

A. Without Ablation.

B. With Reduced Ablation in Comparison to - a Standard Gradient of Remaining Extracellular issue in a Target Area.

12. The Use of a Reverse Gradient of Energy Delivery to Change the Consistency of Soft Tissue by Altering the Extracellular Metabolism of that Tissue.

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Extracellular Tissue in a Target Area.

13. The Use of a Reverse Gradient of Energy Delivery to Change the Overall Function of Soft Tissue by Altering the Extracellular Metabolism of that Tissue.

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Extracellular Tissue in a Target Area.

14. The Use of a Reverse Gradient of Energy Delivery to Change the Growth of Soft Tissue by Altering the Extracellular Metabolism of that Tissue.





BNSDOCID: <WO_____9805380A1_I_>

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Extracellular Tissue in a Target Area.

15. The Use of a Reverse Gradient of Energy Delivery to Change the Intracellular Metabolism of a Soft Tissue Structure.

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Cells in a Target Area.

16. The Use of a Reverse Gradient of Energy Delivery to Change the Extracellular Metabolism of a Soft Tissue Structure.

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Extracellular Tissue in a Target Area.

17. The Use of Electromagnetic Energy with a Reverse Gradient of Energy Delivery to Achieve Molecular Contraction of Collagen and Cellular Contraction of Collagen Containing Tissues Remaining in an Ablation Target.

18. The Use of Electromagnetic Energy to Alter Soft Tissue Volume with a Reverse Cellular and Extracellular Gradient Contraction of Collagen Containing Tissues.

A. Without Ablation.





SDOCID: <WO_____9805380A1_I_>

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Soft Tissue.

19. The Use of Electromagnetic Energy to Alter the Soft Tissue Consistency with a Reversed Cellular and Extracellular Gradient Contraction of Collagen Containing Tissues.

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Soft Tissue.

20. The Use of Electromagnetic Energy to Alter the Overall Function of a Soft Tissue Structure with a Reverse Cellular and Extracellular Gradient Contraction of Collagen Containing Tissues.

A. Without Ablation.

B. With Reduced Ablation in Comparison to a Standard Gradient of Remaining Soft Tissue.

## Additional Claims

1. Additional Claims for Manipulation of RF Parameters (FM, Power), to Achieve the Most Efficient Ionic Magnetic Moment for the Cleavage of Collagen Bonds and the Molecular Contraction of Collagen.

## Miscellaneous Claims





BNSDOCID: <WO_____9805380A1_I_>

1. Manipulation of Electromagnetic Energy to Achieve the Most Efficient Cleavage of Collagen Bonds for Contraction with the Smallest Amount of Thermal Damage to Surface and Adjacent Tissues.

2. The Manipulation of Electromagnetic Energy and Tissue Parameters to Achieve Collagen Contraction with a Minimal Amount of Thermal Damage to Soft Tissue.

3. The Manipulation of Electromagnetic Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissues without Ablation.

4. The Manipulation of Electromagnetic Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissues with Reduced Ablation in Comparison to a Standard Thermal Gradient.

5. The Manipulation of Electromagnetic Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissue with Partial Ablation of Target Tissue, but with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.

6. The Manipulation of Electromagnetic Energy and Tissue Parameters to Achieve Ablation of a Target Tissue without Ablation of Surface and Adjacent Tissues.

7. The Manipulation of Electromagnetic Energy and Tissue Parameters to Achieve Ablation of a Target Tissue with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.





ISDOCID: <WO_____9805380A1_I_>

8. The Manipulation of Electromagnetic Energy and Tissue Parameters to Achieve the Most Efficient Moment of Energy Delivery for the Contraction of Collagen Containing Tissues without Ablation.

9. The Manipulation of Electromagnetic Energy and Tissue Parameters to Achieve the Most Efficient Moment of Energy Delivery for the Contraction of Collagen Containing Tissues with Reduced Ablation in Comparison to a Standard Thermal Gradient.

10. The Manipulation of Electromagnetic Energy and Tissue Parameters to Achieve the Most Efficient Moment of Energy Delivery for the Contraction of Collagen Containing Tissue with Partial Ablation of Target Tissue, but with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.

11. The Manipulation of Electromagnetic Energy and Tissue Parameters to Achieve the Most Efficient Moment of Energy Delivery for Ablation of a Target Tissue without Ablation of Surface and Adjacent Tissues.

12. The Manipulation of Electromagnetic Energy and Tissue Parameters to Achieve the Most Efficient Moment of Energy Delivery for Ablation of a Target Tissue with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.

13. The Manipulation of Laser Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissues with Reduced Ablation in Comparison to a Standard Thermal Gradient.

14. The Manipulation of Laser Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissue with Partial Ablation of





BNSDOCID: <WO_____9805380A1_I_>

Target Tissue, but with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.

15. The Manipulation of Laser Energy and Tissue Parameters to Achieve Ablation of a Target Tissue without Ablation of Surface and Adjacent Tissues.

16. The Manipulation of Laser Energy and Tissue Parameters to Achieve Ablation of a Target Tissue with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.

17. The Manipulation of Ultrasound Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissues with Reduced Ablation in Comparison to a Standard Thermal Gradient.

18. The Manipulation of Ultrasound Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissue with Partial Ablation of Target Tissue, but with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.

19. The Manipulation of Ultrasound Energy and Tissue Parameters to Achieve Ablation of a Target Tissue without Ablation of Surface and Adjacent Tissues.

20. The Manipulation of Ultrasound Energy and Tissue Parameters to Achieve Ablation of a Target Tissue with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.

21. The Manipulation of Microwave Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissues with Reduced Ablation in Comparison to a Standard Thermal Gradient.





SDOCID: <WO_____9805380A1_I_>

22. The Manipulation of Microwave Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissue with Partial Ablation of Target Tissue, but with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.

23. The Manipulation of Microwave Energy and Tissue Parameters to Achieve Ablation of a Target Tissue without Ablation of Surface and Adjacent Tissues.

24. The Manipulation of Microwave Energy and Tissue Parameters to Achieve Ablation of a Target Tissue with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.

25. The Manipulation of Mechanical Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissues with Reduced Ablation in Comparison to a Standard Thermal Gradient.

26. The Manipulation of Mechanical Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissue with Partial Ablation of Target Tissue, but with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.

27. The Manipulation of Mechanical Energy and Tissue Parameters to Achieve Ablation of a Target Tissue without Ablation of Surface and Adjacent Tissues.

28. The Manipulation of Mechanical Energy and Tissue Parameters to Achieve Ablation of a Target Tissue with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.





BNSDOCID: <WO_____9805380A1_I_>

29. The Manipulation of Frictional Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissues with Reduced Ablation in Comparison to a Standard Thermal Gradient.

30. The Manipulation of Frictional Energy and Tissue Parameters to Achieve the Contraction of Collagen Containing Tissue with Partial Ablation of Target Tissue, but with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.

31. The Manipulation of Frictional Energy and Tissue Parameters to Achieve Ablation of a Target Tissue without Ablation of Surface and Adjacent Tissues.

32. The Manipulation of Frictional Energy and Tissue Parameters to Achieve Ablation of a Target Tissue with Reduced Ablation of Surface and Adjacent Tissues in comparison to a Standard Thermal Gradient.

33. The Manipulation of RF Energy and Tissue Parameters to Provide the Most Efficient Magnetic Moment of Energy Delivery for the Contraction of Collagen Containing Tissues without Ablation.

34. The Manipulation of RF Energy and Tissue Parameters to Provide the Most Efficient Magnetic Moment of Energy Delivery for the Contraction of Collagen Containing Tissues with Reduced Ablation in Comparison to a Standard Thermal Gradient.

35. The Manipulation of RF Energy and Tissue Parameters to Provide the Most Efficient Magnetic Moment of Energy Delivery for the Contraction of Collagen Containing Tissue with Partial Ablation of Target Tissue, but with Reduced Ablation of Surface and Adjacent Tissues in Comparison to a Standard Thermal Gradient.





ISDOCID: <WO_____9805380A1_I_>

36. The Manipulation of RF Energy and Tissue Parameters to Provide the Most Efficient Magnetic Moment of Energy Delivery for Ablation of a Target Tissue without Ablation of Surface and Adjacent Tissues.

37. The Use of Thermal Energy as a Magnetocaloric Effect for the Initial Ionic Agitation that Facilitates the RF Polarization of Soft Tissue and Provides the Most Efficient Magnetic Moment with the cast Thermal Damage of Tissue to Achieve a Change in the Surface and Contour of Soft Tissue.

38. The Use of Thermal Energy as a Magnetocaloric Effect for the Initial Ionic Agitation that Facilitates the RF Polarization of Soft Tissue and Provides the Most Efficient Magnetic Moment with the cast Thermal Damage of Tissue to Achieve Contraction of Collagen Containing Tissues.

39. The Use of Thermal Energy to Create the Initial Ionic Agitation Required by RF for the Magnetic Induction of Soft Tissue.

40. The Use of RF Energy for the Magnetic Induction of Soft Tissue Which Created and in Phase Alternating Moment of Ionic Motion that Cleaves the Molecular Cross Links of a Collagen Molecule with Less Thermal Ablation than a Standard Thermal Gradient of Collagen Containing Tissue.

41. The Use of RF Energy for the Magnetic Induction and Polarization of Collagen Containing Tissue for the Creation of an in Phase Alternating Moment of Ionic Motion that Cleaves the Molecular Cross Links of Collagen with Less Thermal Ablation than a Standard Thermal Gradient.

## Tissue Parameters





BNSDOCID: <WO_____9805380A1_I_>

1. Tissue Impedance by Altering the ECF.

2. Tissue Impedance by Altering the ICF.

3. Hydration of skin.

4. Injecting of Conducting Fluid Such as Saline or Injection of Resisting Fluids Such as Glucose.

5. Creation of Inflammatory Edema to Increase ECF.

6. Use of the Scar Maturation Process to Increase Impedance by Decreasing ECF.

7. Mechanical Manipulation to Alter Impedance without Directly Changing the ECF.

   A. Suction cups.

   B. Rollers.

8. Changing the $T_s$ (Shrinkage Temperature of Collagen) by,

   A. Pharmacologic Methods (Wydase).

   B. Low Level Thermal Energy Disruption of Collagen Bonds without Contraction as a Precursor to Magnetic Cleavage and Contraction of Collagen.

   C. Mechanical Manipulation (Massage), to Disrupt Bonds as a Precursor to Magnetic Cleavage, i.e., use of Friction to Decrease





SDOCID: <WO_____9805380A1_I_>

$T_1$ by Directly Cleaving Collagen Bonds and Increasing Ionic Agitation Prior to Magnetic Induction.

More Specifically, the Mechanical Manipulation of Soft Tissue will Alter Tissue Impedance During the Application of RF Energy, but When Applied as Massage During a Precursor Treatment the Following Tissue Parameters Will be Altered.

1. Lower $T_1$ of Collagen by Direct Mechanical Cleavage of Collagen Bonds.

2. Increase Thermal Content of Soft Tissue with Frictional Creation of Heat Which Increases Ionic Agitation Prior to the Magnetic Induction by RF.

D. Facilitation of Surface Energy Losses Through Convection Cooling.

E. Altering the Thermal Conductance of the Epidermis (Stratum Corneum).

Although Hydration will Increase the Electrical Conductance of RF Current Through the Epidermis, a More Significant Effect is the Increase in Thermal Conductance to the Stratum Corneum.

Hydration of the Intracellular (ICF) Fluid of Nonviable and Viable Cellular Components of the Epidermis Occurs by the Uptake of Water in These Keratin Containing Cells. In the Process the Stratum Corneum is Changed into a Thermal Conductor Instead of Typically Functioning as a Thermal Insulator. More Specifically, Keratin is a Poor Thermal and Electrical Conductor. Hydrated Intracellular Keratin is a Better Thermal and Electrical Conductor that





BNSDOCID: <WO_____9805380A1_I_>

Promotes Heat Transfer to Underlying Collagen Containing Tissues and Reduces Intracellular Tissue Impedance.

As a Result, the Improved Transfer of Heat, Through the epidermis facilitates the creation of a transcutaneous reverse thermal gradient.

The foregoing description of a preferred embodiment of the invention has been presented for purposes of illustration and description. It is not intended to be exhaustive or to limit the invention to the precise forms disclosed. Obviously, many modifications and variations will be apparent to practitioners skilled in this art. It is intended that the scope of the invention be defined by the following claims and their equivalents.

What is claimed is:





ISDOCID: <WO_____9805380A1_I_>

## CLAIMS

1. A method for tightening skin, comprising:

providing an electromagnetic energy delivery device with an energy delivery surface;

positioning at least a portion of the energy delivery surface on a skin surface;

delivering electromagnetic energy from the energy delivery surface through the skin surface, through the skin and to an underlying collagen containing tissue;

modifying an impedance of at least a portion of the skin or the underlying collagen containing tissue;

contracting at least a portion of the collagen tissue; and

tightening the surface of the skin.

2. The method of claim 1, wherein the collagen containing tissue is heated to a temperature not exceeding 80 degrees C during a treatment of the collagen containing tissue.

3. The method of claim 1, wherein the collagen containing tissue is heated to a temperature not exceeding 75 degrees C during a treatment of the collagen containing tissue.

4. The method of claim 1, wherein the collagen containing tissue is heated to a temperature not exceeding 70 degrees C during a treatment of the collagen containing tissue.

5. A method for tightening skin, comprising:

providing an electromagnetic energy delivery device;





BNSDOCID: <WO_____9805380A1_I_>

positioning at least a portion of the electromagnetic energy delivery device on a surface of the skin; and

controlling a delivery of a sufficient amount of electromagnetic energy through an epidermis of the surface of the skin and modify an impedance of at least a portion of an underlying collagen containing tissue or the skin without substantially creating cell necrosis in the epidermis, wherein at least a portion of the surface of the skin is tightened.

6. A method for tightening skin, comprising:

providing an electromagnetic energy delivery device;

positioning at least a portion of the electromagnetic energy delivery device on a surface of the skin; and

controlling a delivery of a sufficient amount of electromagnetic energy through an epidermis of the surface of the skin and reconfigure at least a portion of an underlying collagen containing tissue without substantially creating cell necrosis in the collagen containing tissue; and

modifying a thermal conductivity of the skin, wherein at least a portion of the surface of the skin is tightened.





SDOCID: <WO_____9805380A1_I_>

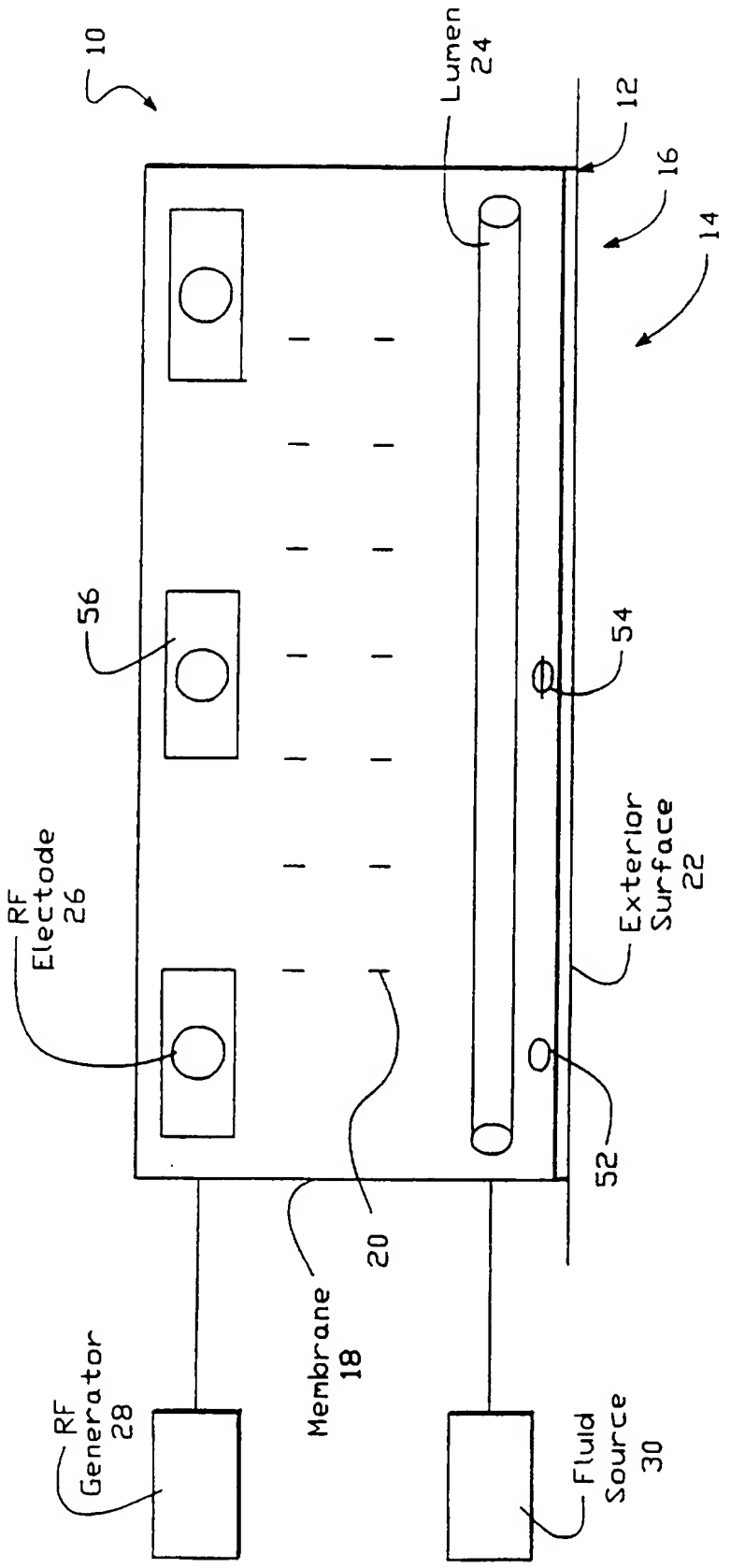



FIG. 1



BNSDOCID: <WO_____9805380A1_I_>

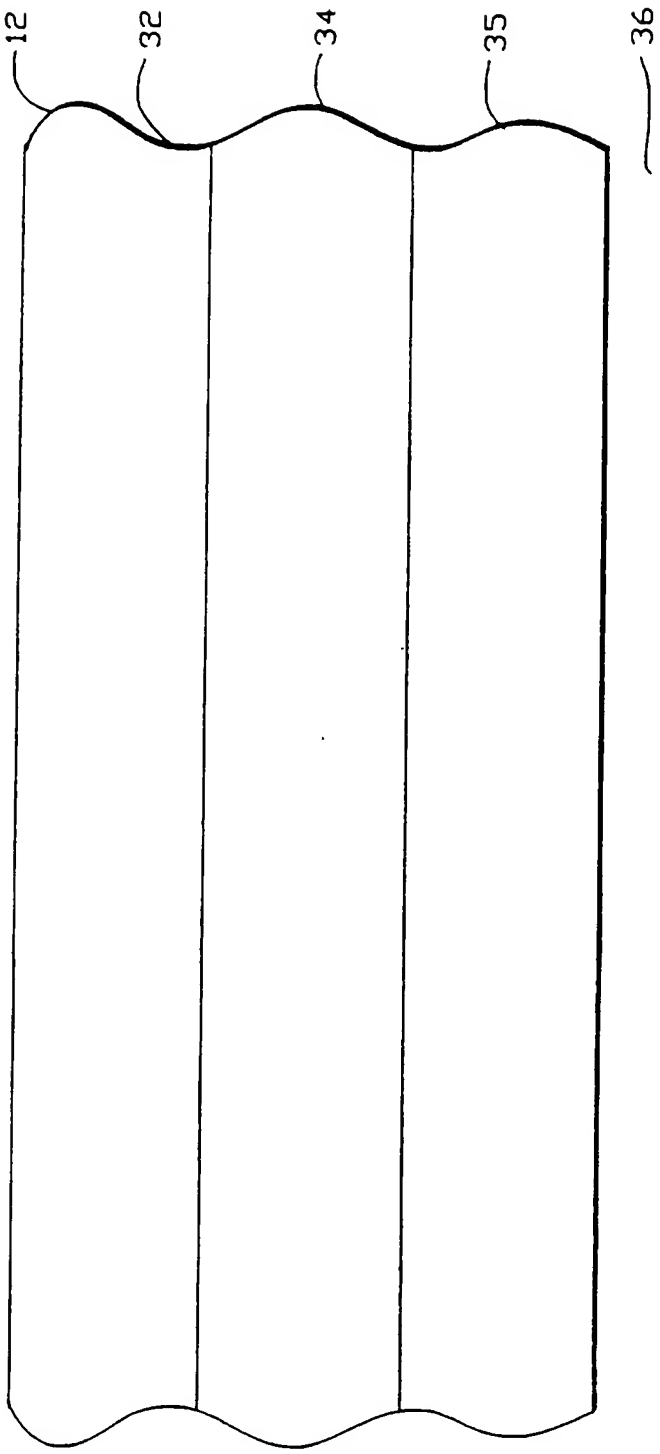



FIG.2



ISDOCID: <WO_____9805380A1_I_>

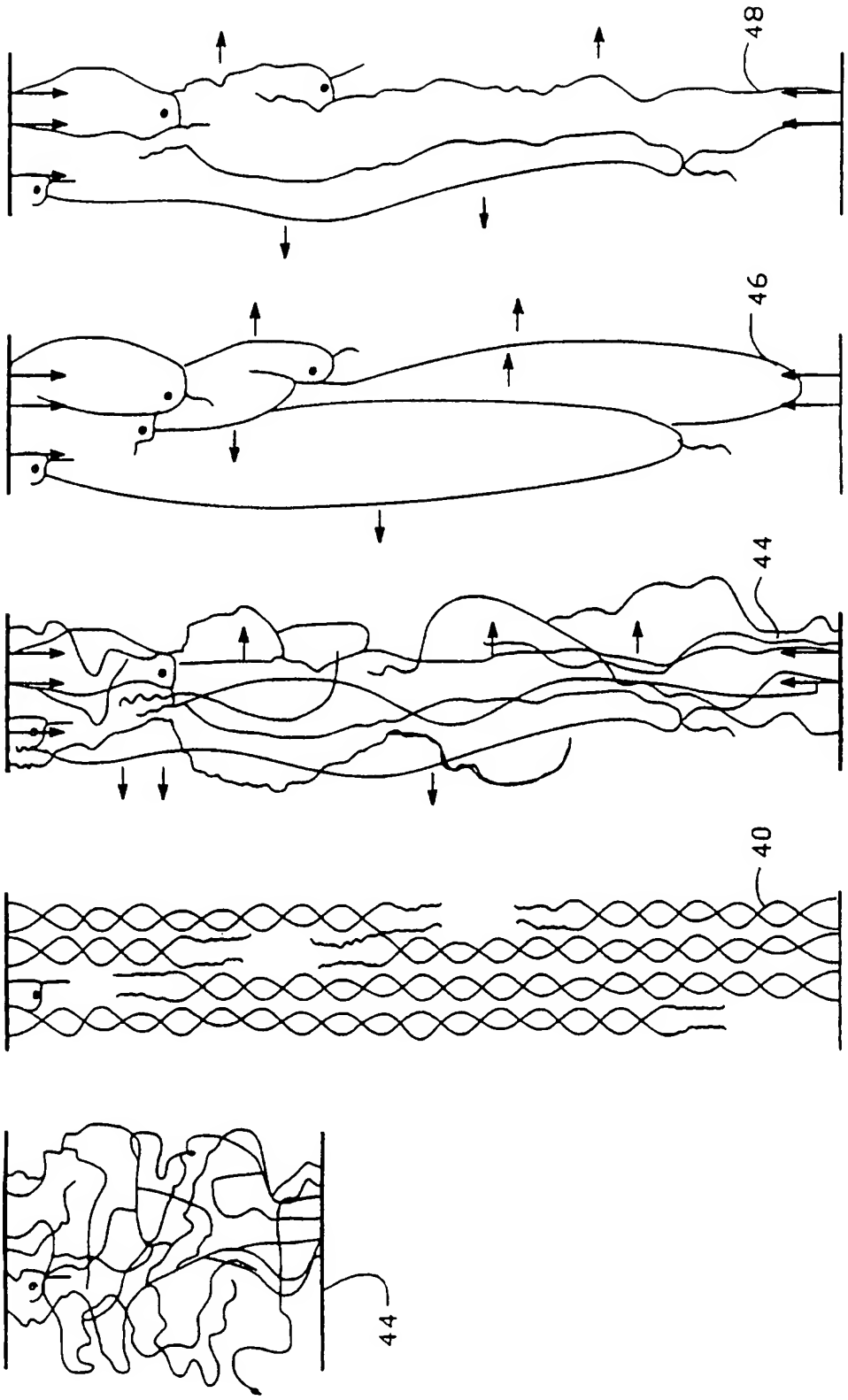



FIG.3



BNSDOCID: <WO_____9805380A1_I_>

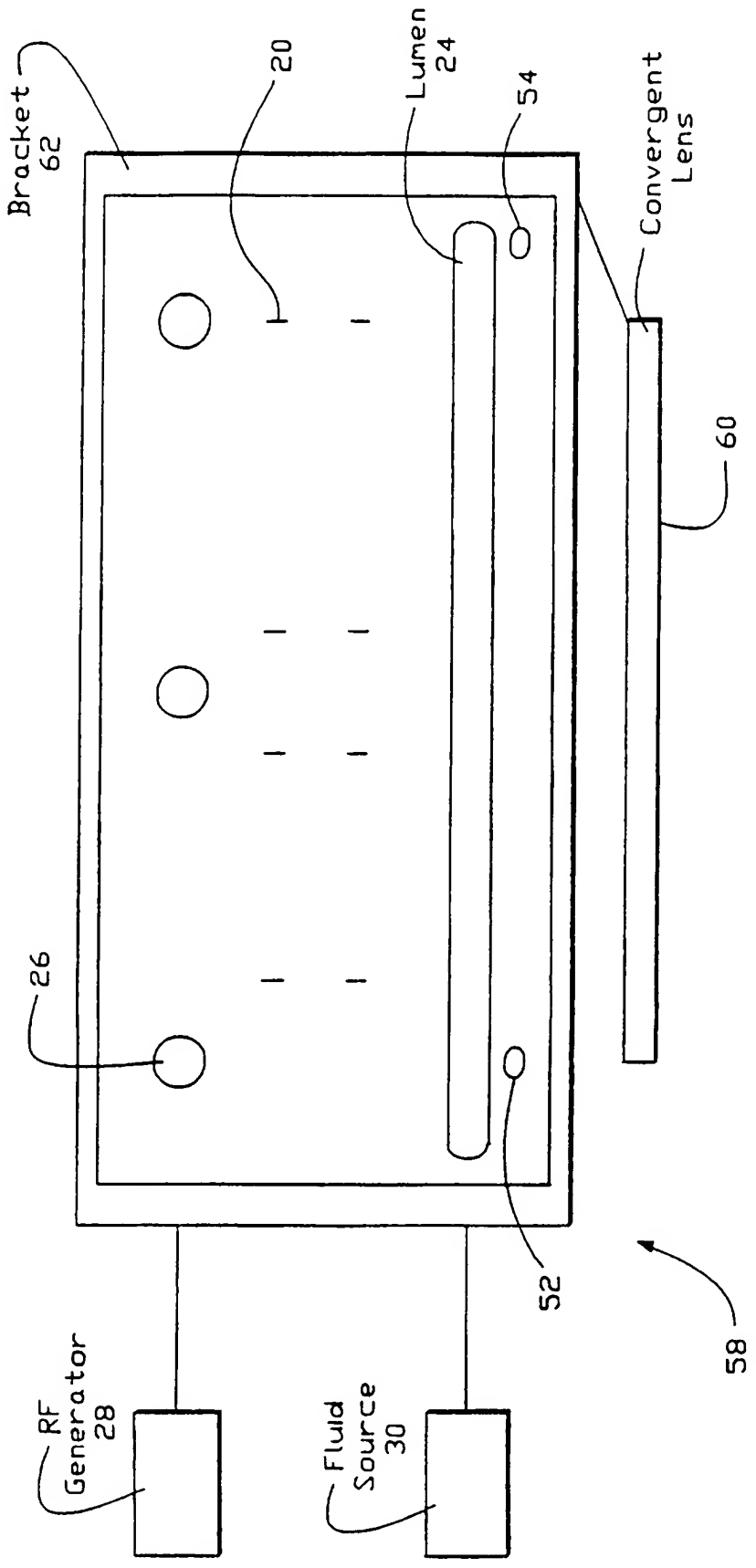



FIG. 4



ISDOCID: <WO_____9805380A1_I_>

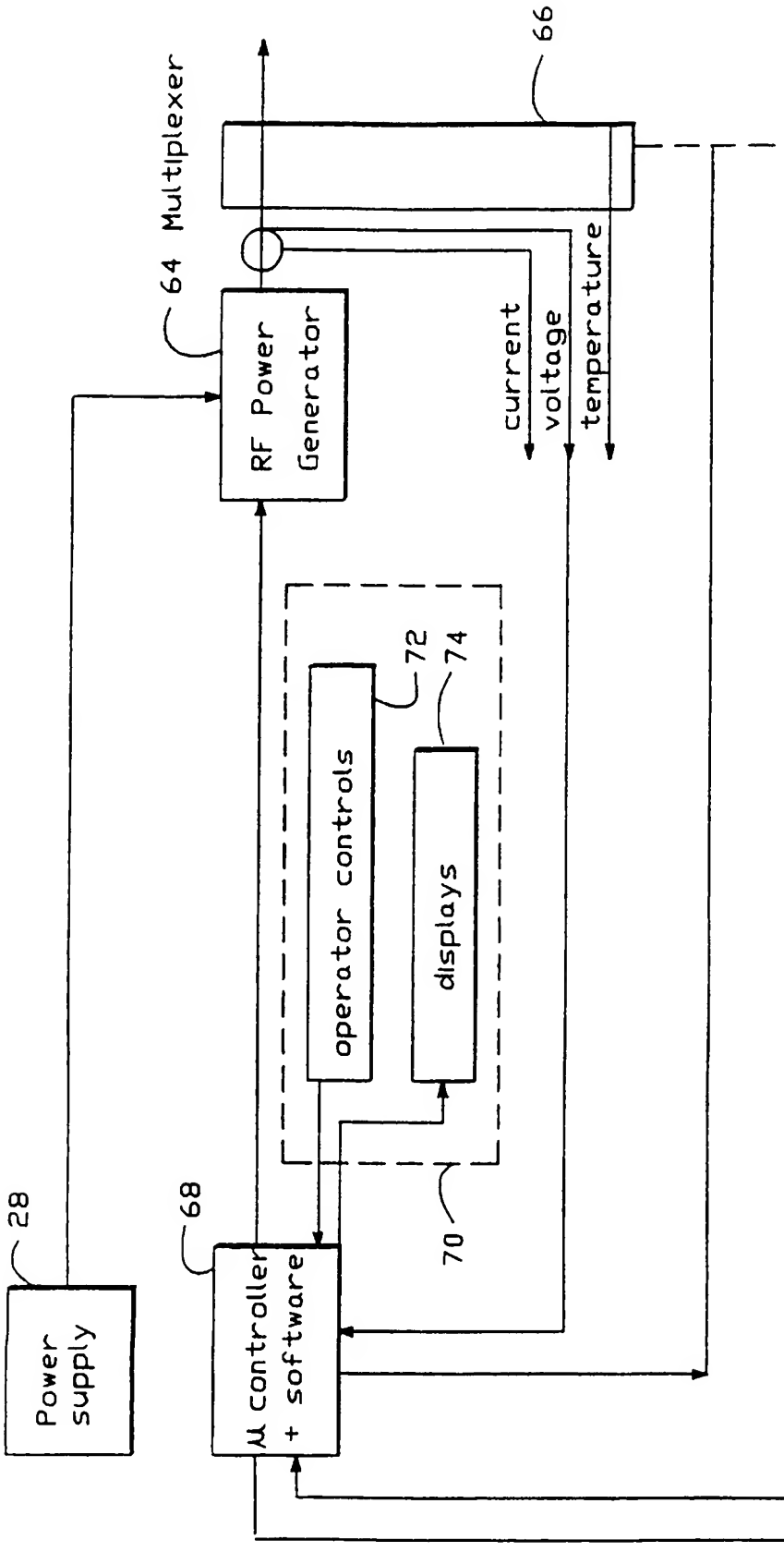



FIG. 5



BNSDOCID: <WO_____9805380A1_I_>

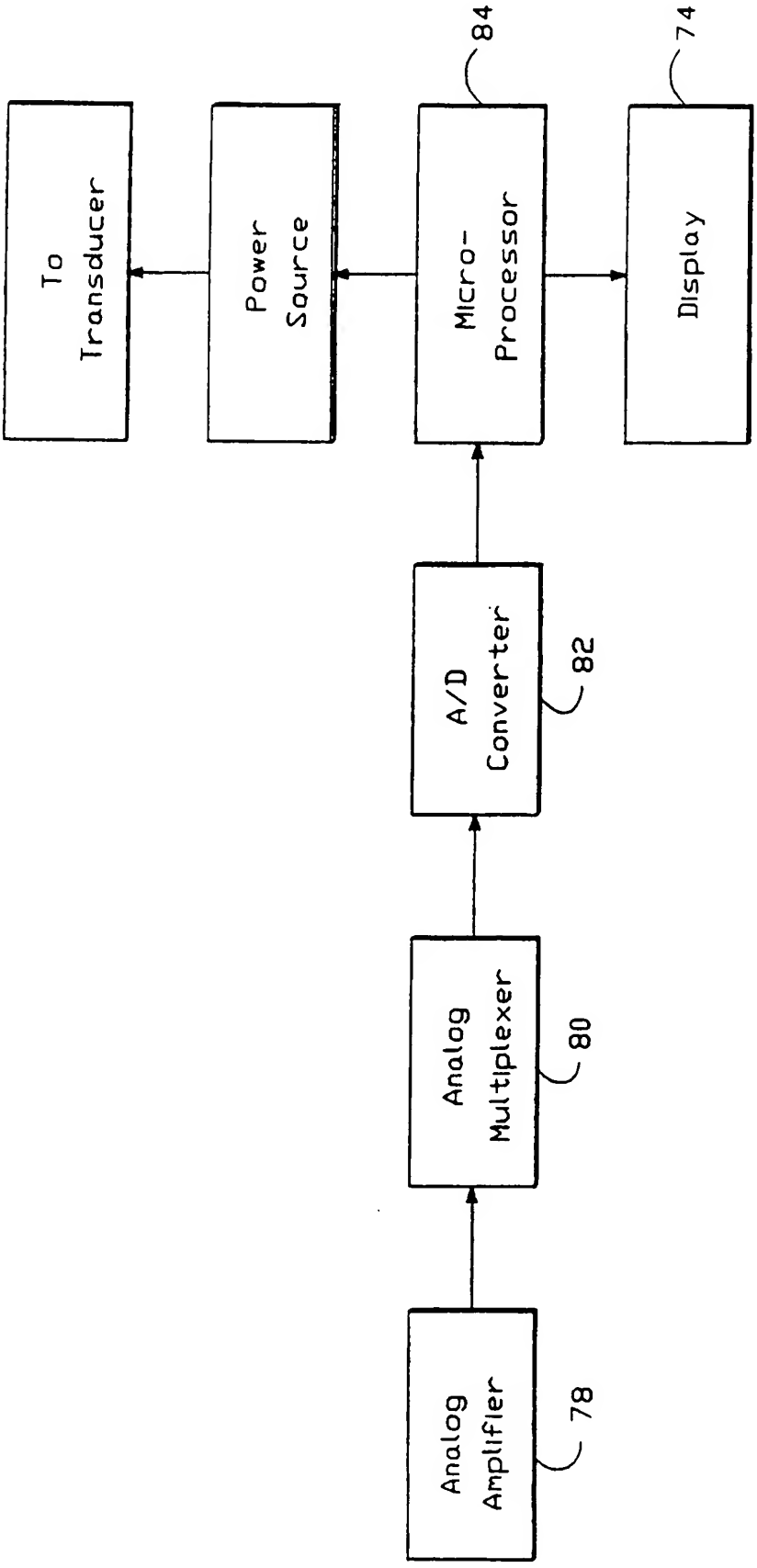



FIG.6



SDOCID: <WO_____9805380A1_I_>

# INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 97/13608

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61N1/40 A61H7/00

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61N A61H

Documentation searched other than minimumdocumentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| P,X | WO 96 34568 A (KNOWLTON) 7 November 1996<br>cited in the application<br>see the whole document | 1,5,6 |
| A,P | US 5 569 242 A (LAX) 29 October 1996<br>see abstract; figure 9 | 1,5,6 |
| A | US 5 304 169 A (SAND) 19 April 1994<br>see abstract | 1,5,6 |
| A | US 4 381 007 A (DOSS) 26 April 1983<br>see column 2, line 15 - line 18<br>see column 1, line 18 - line 35 | 1,5,6 |
| A | WO 91 16942 A (IDESKA) 14 November 1991<br>see abstract | |

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publicationdate of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

2

| Date of the actual completion of theinternational search | Date of mailing of the international search report |
|---|---|
| 7 November 1997 | 17/11/1997 |

| Name and mailing address of the ISA | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+31-70) 340-3016 | Papone, F |

Form PCT/ISA/210 (second sheet) (July 1992)

BNSDOCID: <WO_____9805380A1_I_>

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 97/13608

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---|---|---|
| WO 9634568 A | 07-11-96 | US 5660836 A | 26-08-97 |
| | | AU 5789396 A | 21-11-96 |
| | | AU 1527397 A | 01-08-97 |
| | | WO 9724992 A | 17-07-97 |
| US 5569242 A | 29-10-96 | US 5458596 A | 17-10-95 |
| | | AU 2432195 A | 29-11-95 |
| | | EP 0760626 A | 12-03-97 |
| | | WO 9530373 A | 16-11-95 |
| US 5304169 A | 19-04-94 | US 4976709 A | 11-12-90 |
| | | US 5137530 A | 11-08-92 |
| | | US 5484432 A | 16-01-96 |
| | | US 5618284 A | 08-04-97 |
| | | US 5374265 A | 20-12-94 |
| | | AT 112950 T | 15-11-94 |
| | | AU 673235 B | 31-10-96 |
| | | AU 5935094 A | 16-06-94 |
| | | AU 645513 B | 20-01-94 |
| | | AU 6034290 A | 17-01-91 |
| | | CA 2063245 A | 31-12-90 |
| | | DE 69013508 D | 24-11-94 |
| | | DE 69013508 T | 24-05-95 |
| | | EP 0480995 A | 22-04-92 |
| | | EP 0581339 A | 02-02-94 |
| | | ES 2064745 T | 01-02-95 |
| | | JP 4506312 T | 05-11-92 |
| | | WO 9100063 A | 10-01-91 |
| US 4381007 A | 26-04-83 | CH 656303 A | 30-06-86 |
| | | DE 3215832 A | 18-11-82 |
| | | JP 57183850 A | 12-11-82 |
| WO 9116942 A | 14-11-91 | FR 2661616 A | 08-11-91 |
| | | AU 7891591 A | 27-11-91 |
| | | CA 2063385 A | 04-11-91 |
| | | EP 0481060 A | 22-04-92 |



SDOCID: <WO_____9805380A1_I_>